combination of Compound B and human growth factor has a synergistic effect.

Claims 1 and 2 have been rejected under 35 U.S.C. §101, as being directed to non-statutory subject matter. The examiner states that the claims recite a use without setting forth steps involved in a claimed method or process. This rejection is respectfully traversed.

Claims 1 and 2 have been replaced by new method claims 11 and 12. The new claims are directed to statutory subject matter.

Claims 1-9 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. This rejection is respectfully traversed.

The examiner states that claims 1 and 2 have been rejected as being indefinite because they lack essential steps as claimed in the process of treating wounds, etc. The omitted steps are those whereby the desired outcome and the time for the effective treatment using Component B in combination with human growth factor can be determined. Claim 2 is also indefinite, according to the examiner, because it lacks antecedent basis in Claim 1.

Claims 1 and 2 have been canceled, and new claims 11 and 12 are intended to eliminate any deficiencies in the original claims.

Claim 3 has been rejected as being indefinite, according to the examiner, because it is not clear which pharmaceutical composition is intended for use as a cicatrizant.

Claim 3 has been amended in line with the examiner's helpful suggestion and the limitation "useful as cicatrizants" has been removed therefrom.

Claim 4 has been rejected as being indefinite, according to the examiner, because of the use of the phrase "two active principle are both present".

Claim 4 has been amended per the examiner's suggestion.

Claim 5 has been rejected as being indefinite.

Claim 5 has now been canceled, thus obviating this part of the rejection.

Claims 4-6 have been rejected as being indefinite, according to the examiner, because it is not clear which "pharmaceutical composition" of the dependent claim is intended for using as a cicatrizant.

Claims 4 and 6 have been amended according to the examiner's suggestion. Claim 5 has been deleted.

Claim 7 has been rejected as being indefinite, according to the examiner, because it is not clear which "method" is intended for the treatment of wounds, ulcers, etc., and also because it lacks essential steps as claimed in the process of treating wounds, etc. The omitted steps are those whereby the desired outcome and the time for the effective treatment using Component B in combination with human growth factor can be determined.

Claim 7 has been canceled and its subject matter is recited in new claim 20, which applicants believe addresses the examiner's rejections.

Claims 8-9 have been rejected as being indefinite, according to the examiner, because it is not clear which "method" of the dependent claim is intended for the treatment of wounds, ulcers, etc.

Claims 8-9 have been canceled and new claims 21 and 22 have been added. Applicants believe that the new claims fully address the examiner's rejections.

Claims 7-9 have been rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claim 1 of U. S. Patent No. 5,998,364. The examiner states that the claims are not patentably distinct from one another because claim 7 is directed to the broadest scope of the method of treatment of wounds, ulcers

and other traumatic lesions to any of the tissues in the body. This rejection is respectfully traversed.

The double-patenting rejection appears to be based on the examiner's observation that claim 1 of the '364 patent is broad enough to encompass the process of the presently-claimed invention. However, the examiner's attention is invited to MPEP §804.II, where it states:

> Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or non-statutory double patenting grounds, cannot support a double patenting rejection.

Claims 7-9 have now been cancelled in favor of new claims 20-23. Claims 20-23 require that both Component B and a human growth factor be administered. Claim 1 of the '364 patent does not mention the use of human growth factor. Human growth factor is not "a pharmaceutically acceptable carrier". There is nothing in claim 1 of the '364 patent which would provide any motivation whatsoever to add any human growth factor to the composition used in the method of claim 1. Without motivation to co-administer human growth factor, no *prima facie* case of obviousness has been established by the examiner. As stated in MPEP §804.II.B.1.:

> A double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination.

In a 35 U.S.C. §103 rejection, the examiner would never reject a claim for the administration of A and B based on a reference that only discloses the administration of A. Thus, the same is impermissible in a double patenting analysis.

Furthermore, claim 23 requires that the components be present in synergistic amounts. This further rebuts any *prima facie* case of obviousness. Even if the examiner establishes a *prima facie* case of obviousness for administering the combination of Compound B and human growth factor for wound healing, the synergistic effects of the present invention, which are clearly disclosed in the examples of the present specification, would rebut any such *prima facie* case of obviousness.

The unexpected synergistic effects of the combination of Component B with human growth factor demonstrated in the present specification with respect to their angiogenic effect is also applicable to wound healing as it is well established that angiogenesis is a critical factor

in wound healing. In this regard, attached hereto is a printout from the web site of the Angiogenesis Foundation, found at http://www.angio.org/newsandviews/archive2001/NV_Services_SH.pdf, stating that wound healing is accelerated by enhancing the natural process of angiogenesis. Also attached hereto is an abstract of Pettet et al, "On the role of angiogenesis in wound healing", Proc R Soc Lond B Biol Sci 263(1376):1487-1493 (1996).

For all of these reasons, reconsideration and withdrawal of the double patenting rejection is respectfully urged.

All the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,
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Version with Markings to Show Changes Made

In the Claims

Claims 3 and 4 have been amended as follows:

3 (Amended). ~~Pharmaceutical~~ A pharmaceutical composition ~~useful as cicatrizants~~ comprising Component B and a human growth factor as active principles in combination with a pharmaceutically acceptable carrier.

4 (Amended). ~~Pharmaceutical~~ The pharmaceutical composition according to Claim 3 wherein the two active ~~principle~~ principles are ~~both~~ present in a single administration dose.

6 (~~Amended~~Twice-amended). ~~Pharmaceutical~~ The pharmaceutical composition according to Claim 3 wherein the human growth factor is bFGF or VEGF.

Claims 1, 2, 5 and 7-9 have been deleted.

Claims 10-23 have been added.